

In re Application of:

Hall et al.

Application No.: 09/441,966

Filed: November 17, 1999

Page 3

PATENT

Attorney Docket No.: AERO1120-1

IN THE CLAIMS

Please amend claims 1-4, 7, 10, 15-17, and 19, as set forth below. Please cancel claims 18, 20, and 21 without prejudice, as non-elected claims. Please add new claim 22. The following listing of claims replaces all previous listings.

1. (Currently amended) A method for accelerating the rate of mucociliary clearance in a subject in need of such treatment thereof, comprising administering to the subject an effective mucociliary clearance stimulatory amount of a composition comprising a human Kunitz-type serine protease inhibitor and a physiologically acceptable carrier, wherein the human Kunitz-type serine protease inhibitor is selected from the group consisting of:

MAQLCGL RRSRAFLALL GSLLLLSGVLA -1

ADRERSIHDF CLVSKVVGRC RASMPRWWYN VTDGSCQLFV YGGCDGNSNN 50

YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DSEDHSSDMF 100

NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE 150

ACMLRCFRQQ ENPPLPLGSK VVVLAGLFVM VLILFLGASM VYLIRVARRN 200

QERALRTVWS SGDDKEQLVK NTYVL 225

(SEQ ID NO.:49);

AGSFLAWL GSLLLLSGVLA -1

ADRERSIHDF CLVSKVVGRC RASMPRWWYN VTDGSCQLFV YGGCDGNSNN 50

YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DSEDHSSDMF 100

NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE 150

ACMLRCFRQQ ENPPLPLGSK VVVLAGAVS 179

(SEQ ID NO.:2);

In re Application of:

Hall et al.

Application No.: 09/441,966

Filed: November 17, 1999

Page 4

PATENT

Attorney Docket No.: AERO1120-1

ADRERSIHDF CLVSKVVGRC RASMPRWWYN VTDGSCQLFV YGGCDGNSNN 50
YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DSEDHSSDMF 100
NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE 150
ACMLRCFRQQ ENPPLPLGSK VVVLAGLFVM VLILFLGASM VYLIRVARRN 200
QERALRTVWS SGDDKEQLVK NTYVL 225

(SEQ ID NO.:45);

MAQLCGL RRSRAFLALL GSLLLSGVLA -1

ADRERSIHDF CLVSKVVGRC RASMPRWWYN VTDGSCQLFVYGGCDGNSNN 50
YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DSEDHSSDMF 100
NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE 150
ACMLRCFRQQ ENPPLPLGSK VVVLAGLFVM VLILFLGASM VYLIRVARRN 200
QERALRTVWS FGD 213

(SEQ ID NO.:47);

ADRERSIHDF CLVSKVVGRC RASMPRWWYN VTDGSCQLFV YGGCDGNSNN 50
YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DSEDHSSDMF 100
NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE 150
ACMLRCFRQQ ENPPLPLGSK VVVLAGLFVM VLILFLGASM VYLIRVARRN 200
QERALRTVWS SGDDKEQLVK NTYVL 225

(SEQ ID NO.:71);

In re Application of:

Hall et al.

Application No.: 09/441,966

Filed: November 17, 1999

Page 5

PATENT

Attorney Docket No.: AERO1120-1

ADRERSIHDF CLVSKVVGRC RASMPRWWYN VTDGSCQLFV YGGCDGNSNN 50
YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DSEDHSSDMF 100
NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE 150
ACMLRCFRQQ ENPPLPLGSK VVVLAGLFVM VLILFLGASM VYLIRVARRN 200
QERALRTVWS FGD 213

(SEQ ID NO.:70);

IHDF CLVSKVVGRC RASMPRWWYN VTDGSCQLFV YGGCDGNSNN 50
YLTKEECLKK CATV 64

(SEQ ID NO.:4);

CLVSKVVGRC RASMPRWWYN VTDGSCQLFV YGGCDGNSNN 50
YLTKEECLKK C 61

(SEQ ID NO.:5);

YEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE 150
ACMLRCFRQ 159

(SEQ ID NO.:6);

CTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE 150
ACMLRC 156

(SEQ ID NO.:7);

In re Application of:

Hall et al.

Application No.: 09/441,966

Filed: November 17, 1999

Page 6

PATENT

Attorney Docket No.: AERO1120-1

IHDF CLVSKVVGRC RASMPRWWYN VTDGSCQLFV YGGCDGNSNN 50

YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DSEDHSSDMF 100

NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE 150

ACMLRCFRQ 159

(SEQ ID NO.:3);

CLVSKVVGRC RASMPRWWYN VTDGSCQLFV YGGCDGNSNN 50

YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DSEDHSSDMF 100

NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE 150

ACMLRC 156

(SEQ ID NO.:50);

ADRERSIHDF CLVSKVVGRC RASMPRWWYN VTDGSCQLFV YGGCDGNSNN 50

YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DSEDHSSDMF 100

NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE 150

ACMLRCFRQQ ENPPLPLGSK VVVLGAVS 179

(SEQ ID NO.:1);

ADRERSIHDF CLVSKVVGRC RASMPRWWYN VTDGSCQLFV YGGCDGNSNN 50

YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DSEDHSSDMF 100

NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE 150

ACMLRCFRQQ ENPPLPLGSK 170

(SEQ ID NO.:52); and

In re Application of:

Hall et al.

Application No.: 09/441,966

Filed: November 17, 1999

Page 7

PATENT

Attorney Docket No.: AERO1120-1

ADRERSIHDF CLVSKVVGRC RASMPRWWYN VTDGSCQLFV YGGCDGNSNN 50

YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DS 92

(SEQ ID NO.:8),

thereby accelerating the rate of mucociliary clearance.

2. (Currently amended) The method according to claim 1 or 22, wherein the composition is administered to the lung airways.

3. (Currently amended) The method according to claim 1 or 22, wherein said composition is administered directly by aerosolization.

4. (Currently amended) The method according to claim 1 or 22, wherein said composition is administered directly as an aerosol suspension into the ~~mammal's~~ subject's respiratory tract.

5. (Original) The method according to claim 4, wherein said aerosol suspension includes respirable particles ranging in size from about 1 to about 10 microns.

6. (Original) The method according to claim 4, wherein said aerosol suspension includes respirable particles ranging in size from about 1 to about 5 microns.

7. (Currently amended) The method according to claim 4, wherein said aerosol suspension is delivered to said subject by a pressure driven nebulizer or administered as dry powder.

8. (Original) The method according to claim 4, wherein said aerosol suspension is delivered to said subject by an ultrasonic nebulizer.

In re Application of:

Hall et al.

Application No.: 09/441,966

Filed: November 17, 1999

Page 8

PATENT

Attorney Docket No.: AERO1120-1

9. (Original) The method according to claim 4, wherein said aerosol suspension is delivered to said subject by a non-toxic propellant.

10. (Currently amended) The method to claim 1 or 22, wherein said carrier is a member selected from the group consisting of a physiologically buffered solution, an isotonic saline, normal saline, and combinations thereof.

11-14. (Canceled).

15. (Currently amended) The method according to claim 1 or 22, wherein the human Kunitz-type serine protease inhibitor is

ADRERSIHDF CLVSKVVGRC RASMPRWWYN VTDGSCQLFV YGGCDGNSNN 50
YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DS 92

(SEQ ID NO.:8).

16. (Currently amended) The method according to claim 1 or 15, wherein the human Kunitz-type serine protease inhibitor is glycosylated.

17. (Currently amended) The method according to claim 1 or 15, wherein the human Kunitz-type serine protease inhibitor contains at least one intra-chain cysteine-cysteine disulfide bond.

18. (Withdrawn) The method according to claim 1, wherein the Kunitz-type serine protease inhibitor contains at least one intra-chain cysteine-cysteine disulfide bond selected from the cysteine-cysteine paired groups consisting of CYS11-CYS61, CYS20-CYS44, CYS36-CYS57, CYS106-CYS156, CYS115-CYS139, and CYS131-CYS152 for any of
SEQ ID NO.: 49, SEQ ID NO.: 2, SEQ ID NO.: 45, SEQ ID NO.: 47, SEQ ID NO.: 71,

In re Application of:

Hall et al.

Application No.: 09/441,966

Filed: November 17, 1999

Page 9

PATENT

Attorney Docket No.: AERO1120-1

SEQ ID NO.: 70, SEQ ID NO.: 3, SEQ ID NO.: 50, SEQ ID NO.: 1, and SEQ ID NO.: 52, wherein the cysteine residues are numbered according to the amino acid sequence of SEQ ID NO.: 52.

19. (Currently amended) The method of claim 1 or 22, wherein the human Kunitz-type serine protease inhibitor contains at least one intra-chain cysteine-cysteine disulfide bond selected from the cysteine-cysteine paired groups consisting of CYS11-CYS61, CYS20-CYS44, CYS36-CYS57, for any of SEQ ID NO.: 4, SEQ ID NO.: 5, and SEQ ID NO.: 8, wherein the cysteine residues are numbered according to the amino acid sequence of SEQ ID NO.: 52.

20. (Withdrawn) The method according to claim 1, wherein the Kunitz-type serine protease inhibitor contains at least one intra-chain cysteine-cysteine disulfide bond selected from the cysteine-cysteine paired groups consisting of CYS106-CYS156, CYS115-CYS139, and CYS131-CYS152 for any of SEQ ID NO.: 6, and SEQ ID NO.: 7, wherein the cysteine residues are numbered according to the amino acid sequence of SEQ ID NO.: 52.

21. (Withdrawn) The method according to claim 1, wherein the human Kunitz-type serine protease inhibitor contains at least one intra-chain cysteine-cysteine disulfide bond selected from the cysteine-cysteine paired groups consisting of CYS11-CYS61, CYS20-CYS44, CYS36-CYS57, wherein the cysteine residues are numbered according to the amino acid sequence of SEQ ID NO.: 52.

22. (New) The method according to claim 1, wherein the rate of mucociliary clearance is increased by more than about 30 per cent, compared with the rate of mucociliary clearance in the absence of the treatment.